

**Rejections Under 35 U.S.C. 112, First Paragraph**

The Examiner rejected claims 1-4, 6, 7, 11, 12, 15, 21, 30, 31, 39-47, 54-56 and 72 under 35 U.S.C. 112, first paragraph, as not enabled. Applicants respectfully request reconsideration of the rejection in view of the amendments to the claims and the statements below.

Applicants have canceled claims 1-4, 6, 7, 11, 12, 15, 21, 30, 31, 43, 45, 47, 55 and 72. The remaining claims relate to CUB domain sequences, and have been amended to reduce the scope of the claims by recitation that the claimed nucleic acid molecules consist essentially of recited sequences, rather than comprise such sequences.

The Examiner stated that one of skill in the art could not readily predict the function of sequences comprising CUB domains because the application teaches that VEGFX protein including a CUB domain, is stimulatory, not inhibitory.

Applicants respectfully urge reconsideration based on the amendments made to the claims. Further, Applicants note that the specification is quite clear in its teaching of the inhibitory function of the identified CUB domain. Pages 18-20 contain recitations of the CUB domain function and its uses. Figures 26 and 27 show the sequence of a CUB domain nucleic acid and polypeptide, and its expression. Figure 28 demonstrates the inhibitory effect that the CUB domain protein has on HUVEC proliferation. Figure 35 shows the results of cytotoxicity testing of the CUB domain polypeptide. Accordingly, Applicants have provided ample guidance to one of ordinary skill in the art to enable the use of the CUB domain nucleic acid sequences as presently claimed.

Accordingly, Applicants respectfully request that the Examiner withdraw the rejections made under 35 U.S.C. §112, first paragraph, for lack of enablement.

**Rejections Under 35 U.S.C. §112, Second Paragraph**

The Examiner rejected claims 4, 42, 43, 45-47, 54, 55 and 72 under 35 U.S.C. §112, second paragraph.

Applicants have canceled these claims. Accordingly, Applicants respectfully request that the Examiner withdraw the rejections made under 35 U.S.C. §112, second paragraph.

**Rejections Under 35 U.S.C. §102(e)**

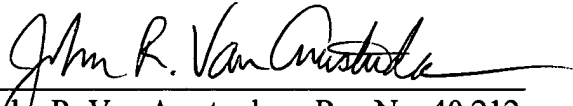
The Examiner rejected claims 1-4, 6, 7, 11, 12, 15, 21, 30, 31, 39-47, 54-56 and 72 under 35 U.S.C. 102(e) as anticipated by US patent 6,391,311. This patent teaches VEGF-E, a region of which is identical to Applicants' VEGF-X sequences.

Applicants have canceled claims pertaining to VEGF-X, but have maintained claims directed to CUB domain. As noted by the Examiner on page 4 of the Office Action, the CUB domains identified in the '311 patent are different from that identified by Applicants. Accordingly, in view of the amendments made to the claims and the differences in the teachings of the '311 patent as compared to the amended claims, Applicant asserts that the '311 patent does not anticipate the claimed invention. Reconsideration is respectfully requested.

**Summary**

Applicants respectfully request reconsideration of the claims in view of the amendments and reasoned statements made above. If the Examiner wishes to advance the prosecution, or if the amendment is defective or unclear, then the Examiner is invited to telephone the undersigned at the telephone number listed below.

Respectfully submitted,

  
John R. Van Amsterdam, Reg No. 40,212  
Wolf, Greenfield & Sacks, P.C.  
600 Atlantic Avenue  
Boston, Massachusetts 02210  
Telephone: (617) 720-3500

Docket No. B00192.70011.US  
Dated: November 12, 2002  
x11/10/02

**MARKED-UP CLAIMS**

39. (twice amended) An isolated nucleic acid molecule encoding a polypeptide having a CUB domain, said polypeptide [comprising] consisting essentially of the amino acid sequence of SEQ ID NO:26.
40. (twice amended) An isolated nucleic acid molecule encoding a polypeptide having a CUB domain, said polypeptide [comprising] consisting essentially of the amino acid sequence of SEQ ID NO:27.
41. (twice amended) An isolated nucleic acid molecule according to claim 40, [comprising] consisting essentially of the nucleotide sequence of SEQ ID NO:28.
42. (twice amended) An isolated nucleic acid molecule according to claim 41, [comprising] consisting essentially of the nucleotide sequence of SEQ ID NO:29.
56. (twice amended) An isolated nucleic acid molecule encoding a polypeptide [comprising] consisting essentially of the amino acid sequence of SEQ ID NO:26 for use as a medicament.